Advances in the Treatment of Multiple Sclerosis

IN THE PAST DECADE there has been a dramatic evolution in the treatment and management of multiple sclerosis. In the past, the major management issue for clinicians was whether "to tell or not to tell the patient" (the diagnosis). Now clinicians and patients are asking, "With which drug therapy do we start and when?"

Both scientific and technical advances have contributed to this change. Through studies of immunopathogenic mechanisms, we have enhanced our understanding of the role of activated T cells, proinflammatory and anti-inflammatory cytokines, and interactions between T-cell receptors, antigen-presenting cells, and major histocompatibility structures (trimolecular complex). This has led to new treatment approaches targeted to specific pathogenic mechanisms. These include T-cell vaccination, monoclonal antibodies directed at the trimolecular complex, and immune modulators such as the interferons or roquinimex, a drug with effects on diverse immune cell populations. Magnetic resonance imaging has added substantially to the understanding of multiple sclerosis disease activity and provides a marker of disease progression.

As of this writing, there are two Food and Drug Administration (FDA)–approved drugs available for patients with relapsing multiple sclerosis. Both are interferon betas.[1,2] The first product, Betaseron, produced by Berlex, became available in 1993. By the spring of 1996, Avonex, produced by Biogen, was also approved. In September 1996, the advisory panel for the FDA reviewed a phase III clinical trial with copolymer 1 and recommended approval.[3] Thus, by 1997 it is probable that at least three drugs will be on the market in the United States designed to alter the natural history of multiple sclerosis.

With so many new and exciting developments, investigators and clinicians tend to focus on disease prevention. Consensus panels have met to discuss which medications will decrease the likelihood of relapse, yet not produce adverse side effects; which will slow progression; and which patients are most suitable to begin therapy.[4] While there is great interest in altering the disease course, patients also need help in dealing with the daily obstacles multiple sclerosis presents to functional activities and quality of life. The review by Drs Andersson and Goodkin elsewhere in this issue addresses this need.[5]

Multiple sclerosis is exceptionally clinically variable. Patients' symptoms range from cognitive loss to urinary incontinence. Daily issues include how to combat stiffness, weakness, painful spasms, fatigue, mood swings, and depression.

Drs Andersson and Goodkin summarize the major pharmacologic treatments available for the amelioration of multiple sclerosis symptoms.[5] Their review also highlights important changes that have occurred in the management approach to this disease. A major advance in patient management is that at most multiple sclerosis centers, patients are cared for by a team of physicians, nurses, physical and occupational therapists, and social workers. This integrated approach enhances function and quality of life. A second issue concerns the assessment of quality of life. Instruments are being developed and tested to measure quality-of-life changes as an important end point for clinical trials.[6]

Physical therapy and exercise are effective means of combatting spasticity. Medication is also often necessary. New pharmacologic therapies for this problem include the intrathecal administration of baclofen and the oral agent tizanidine hydrochloride. Tizanidine, which is shortly expected to receive FDA approval, acts as an agonist at noradrenergic receptors (differing from the mechanism of action of baclofen, which is at the γ-aminobutyric acid receptor) and has been shown to be effective for spasticity in multicenter trials in North America and in Europe.[7,8]

Patients with multiple sclerosis frequently experience problems related to bladder and bowel dysfunction. These include both the failure to store and the failure to empty. In the case of bladder dysfunction, intermittent catheterization, as the authors point out, can give patients what they want most, a sense of control over their lives.

Fatigue is another incapacitating symptom in multiple sclerosis. It interferes with patients' activities of daily living, is a frequent reason for applying for disability, and cannot easily be pigeonholed as depression or weakness. It is difficult to treat, but as reviewed in this issue, the administration of amantadine hydrochloride may sometimes help. Recently aerobic exercise was shown to help multiple sclerosis patients with spasticity and fatigue and to increase patients' sense of well-being. A gradual, individually tailored exercise program and physical therapy should be incorporated into any treatment program for fatigue and spasticity.[9]

Psychiatric symptoms and, in particular, depression are common problems. Multiple sclerosis patients are at a substantially greater risk for suicide than the general population. The early recognition and treatment of depression, anxiety, and bipolar illness can reduce symptoms of pain, fatigue, and decreased disability and open up treatment options (such as with an interferon β) that would otherwise be contraindicated.

One of the current myths about multiple sclerosis is that it is not associated with pain. Pain is frequent, however, and can occur as painful spasms, trigeminal neuralgia, aching, burning shocklike sensations, itching, and tightness. The appropriate treatment of acute and chronic pain syndromes not only lessens pain but can have added effects of enhancing mood and reducing fatigue.

The decade of the brain has proved an especially exciting time for those involved in the care of multiple sclerosis patients. Treatment strategies for enhancing quality of life, modifying symptoms, and altering the natural history of the disease are being actively pursued by clinical investigators, pharmaceutical companies, and national funding agencies. The future for patients with this disease has brightened.

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